

**ABSTRACT****ANTI-HEPATITIS C VIRUS ACTIVITY OF 96% ETHANOLIC EXTRACT OF *Phyllanthus niruri* L. HERB IN COMBINATION WITH SIMEPREVIR BY IN VITRO CULTURE CELL**

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Hepatitis C virus (HCV) infection is the main cause of chronic liver disease, such as cirrhosis and liver cancer. Currently, the standard of hepatitis C virus treatment has been highly developed and achieved the level of Sustained Virological Response (SVR) more than 90%. However, the possibility of resistance and the high cost of treatment also need to be considered. This is due to the fact that both of them are one of the causes of hepatitis C therapy failure, especially in populations with relatively low income. Therefore, it is necessary to develop safe, inexpensive and more effective drug therapy for HCV infection. The current study, we conducted an anti-hepatitis C activity test from the ethanol extract of *Phyllanthus niruri* L. by in vitro culture cells using Huh7it cells. The results were found that  $IC_{50}$  of *P. niruri* is  $6.2 \pm 0.6$   $\mu\text{g} / \text{ml}$  which worked more dominantly in the entry step stage of HCV life cycle based on the MOA (Mode of Action) analysis. In addition, combination test of *P. niruri* and anti-hepatitis C drug of simeprevir was also carried out by adding 25  $\mu\text{g}/\text{ml}$  of *P. niruri* extract and further confirm with the Chou-Talalay method analysis. The result of the combination test by adding 25  $\mu\text{g}/\text{ml}$  extract was found that *P. niruri* extract is able to increase an activity of simeprevir up to 3-fold ( $IC_{50}$ :  $3.4 \pm 1.1$  nM) compared to a single treatment of simeprevir ( $IC_{50}$ :  $10.8 \pm 1.3$  nM). Besides, the result of Chou-Talalay method was found that *P. niruri* extract is able to increase an activity of simeprevir up to 2-fold ( $IC_{50}$ :  $4.0 \pm 0.1$  nM) compared to a single treatment of simeprevir ( $IC_{50}$ :  $8.0 \pm 0.2$  nM). In addition, the results of the combination test also demonstrated that *P. niruri* extract worked synergistically with simeprevir as indicated by the Combination Index (CI) less than 1 (0.865). To ensure the safety of all samples, a cytotoxicity test was conducted and the results shown that all of the samples were not cytotoxic as indicated by the